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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/066,496

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Eldon Emberly

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02/28/2006

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EXAMINER

MORAN, MARJORIE A

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 02/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/066,496	Applicant(s) EMBERLY ET AL.	
	Examiner Marjorie A. Moran	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 and 28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____

- 4) ☒ Interview Summary (PTO-413) *Interview date: 10/12/05*
Paper No(s)/Mail Date: 10/12/05.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Specification

The disclosure is objected to because of the following informalities: the phrase "incorporated herein by reference" is repeated in lines 13-14 on page 17.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

The rejection under 35 USC 101 is hereby withdrawn in view of the amendment filed 11/23/05 and the interpretation of "representing" as meaning "displaying." See below. Applicant is advised that a different meaning for the term and/or an amendment to claim 1 removing a step of "representing" or displaying may result in reinstatement of this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Steps of identifying sets of stacks that have no known counterpart, and of “representing” backbone configurations which have been thus identified, as recited in amended claim 1, are new matter. The original claims did not recite any steps of identification or representation. The originally filed specification, on page 7, provides support for steps (a) through (c) of claim 1, but not for newly added steps (d) and (e). Page 22, lines 17-22 of the originally specification, discloses that a **goal** of a disclosed method was to “identify stacks with no *natural* counterparts as candidates for the design of *novel protein folds*” (emphases added by examiner), and further discloses that a designability calculation was performed on an ensemble of helical structures. Figure 2 shows the results of the calculation. The ensemble of helical structures of lines 20-21 corresponds to the “set of stacks comprising ...secondary structural elements” as recited in step (b) of amended claim 1, and the “designability calculation ...using hydrophobic energy” of lines 19-20 corresponds to “evaluating designability” of step (c) of amended claim 1. It is not clear that the “designability calculation” is the same as or inherently includes any step of “identifying” stacks that have no “known” counterpart. The specification does not specifically disclose such a step anywhere, nor does it disclose, generally, a step of comparing stacks to “known” counterparts such those without known counterpart may be identified. Page 22, lines 6-16 does disclose comparing natural helical bundles to calculated (representative) helical stacks, but specifically states that the results indicate/identify those stacks which HAVE counterparts to the natural structures. This is the opposite of the claimed limitations. While it is acknowledged that the goal of the method may have been to identify stacks

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with no natural counterparts, the specification fails to specifically disclose a step of performing an identification step of stacks, *based on an evaluated designability, that have no known counterparts*. With regard to a step of "representing" an identified backbone configuration, Figure 2 merely shows the results of a designability calculation, NOT the results of a comparison and/or identification step. Nowhere does the originally filed specification disclose representation, display, or output of the results of an identification step similar to that recited in amended claim 1.

In the response filed 11/23/05, applicant points to pages 8, 9, and 22 for support for the amendment. Pages 8 and 9 fail to disclose any steps of identification, comparison, or any steps of representation, display or output which may be correlated to new steps (d) and (e) of claim 1. Page 22 does not provide specific support for an identification step, and fails to provide any support for a step of representing the results of an identification step, as set forth above. Thus, applicant's arguments with regard to support are not persuasive and the claims recite new matter for the reasons set forth above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-25 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

All rejections made under 35 USC 112 which are not reiterated below are hereby withdrawn.

Claim 1 recites a step of identifying stacks with no “known counterpart”. It is unclear what is intended as a “known” counterpart; i.e. structures in “known” proteins; any “known” tertiary configuration of a peptide or isolated domain or subunit of a protein, a specific domain (e.g. a “counterpart” domain only) of a “known” protein, etc. In the response filed 11/23/05, applicant states that the “relative limitations” of the term “known” in step (d) would clearly be appreciated by one of skill in the art. The specification does not clearly define a “known counterpart” anywhere. Further, the term “known” does not appear to be a relative one – if a protein or peptide configuration can be found in the PDB or other prior art, one skilled in the art would consider it to be “known”. However, one skilled in the art would not know what is intended as a “counterpart” and therefore would not know what is intended for a “known counterpart”. As it is unclear what is intended to be a “known counterpart” to an evaluated stack, claim 1 is indefinite.

Claim 1 recites a step of “representing” backbone configurations, but it is not clear in what way the configurations are to be “represented”. It is unclear whether applicant intends to “represent” the configurations mathematically, or via some other series of characters, or intends a graphical display, or perhaps intends some sort of substitution, etc.. As it is unclear what is intended by “representing”, the claims are indefinite. For statutory and written description purposes, the term has been

interpreted by the examiner to mean “displaying”; however, it is not clear that this is the meaning actually intended by applicant. Clarification is requested.

Claim 1 recites the term “based on” in step (d). It is unclear what parameters of designability are to be considered, and to what degree, for a identification to be “based on” an evaluated designability, therefore the claim is indefinite.

Claim 9 limits step (b) of claim 1 to “include” a generation step. It is unclear whether the step recited in claim 9 is intended to replace step (b) of claim 1 or be an additional step. If the latter, then this rejection may be overcome by inserting –further— before “includes” in line 1.

Claim 13 recites a step of “applying a predetermined constraint” but fails to recite to what the constraint is to be applied; i.e. the generation step itself, the set of stacks generated, or the secondary structural elements, of step (b) of claim 1. Claim 13 further recites a step of confirming that each stack of a set does not “exceed said predetermined constraint”, which is nonsensical. If a constraint has been applied to a set of data, then the results necessarily meet or fall within the bounds of the constraint; i.e. they inherently can not “exceed” the applied constraint. If the data is merely COMPARED to a constraint (e.g. a threshold), then one may subsequently select data which fall within (or not) the bounds of that constraint (e.g. below or above the threshold) and may confirm that the selected data does indeed meet the criteria of the constraint. Steps of comparison to a constraint and consequent confirmation of data which have been selected are not usually considered by those skilled in the art to be the same as *application* of a constraint, wherein application implies that any resulting data

is necessarily that which meets the constraint. As it is unclear what steps are actually intended by applicant with regard to "applying" a constraint and "confirming" data, claim 13 is indefinite.

Claim 13 recites that a stack not meeting a constraint "is discarded". It is unclear whether applicant intends an active step of discarding data, or merely intends to limit the data or constraint in some way. As the limitation is unclear, the claim is indefinite. If applicant intends an active method step, then this rejection may be overcome by rewriting the claim such that all verbs are recited in active voice.

Claim 13 recites the phrase "each said stack of the set" in line 2, which lacks antecedent basis. Parent claim 1 recites generating a "set of stacks" in step (b), but does not recite an individual stack (i.e. antecedent basis for "said stack") anywhere.

Claim 14 limits the predetermined constraint of claim 13 to be a distance between "connected helices". As no helices are recited in any parent claim, it is unclear what the predetermined constraint is actually intended to be in the claimed method. As the further limitation intended for the method of claim 1 and/or 13 is unclear, claim 14 is indefinite.

Claim 16 limits the method of claim 9 to be one wherein a plurality of stacks "are generated". It is unclear if applicant intends to actually generate a plurality of stacks, as would be indicated by an active method step, or merely intends to limit the stacks in some manner. As the limitation intended is unclear, claim 16 is indefinite.

Claim 16 recites that each stack is "based on" selected starting coordinates. It is unclear what parameters are to be considered, and to what degree, in order to

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determine if a stack is “based on” selected starting coordinates, therefore claim 16 is indefinite.

Claim 18 recite the phrase “wherein further including a step” which is nonsensical. It is unclear whether applicant intends to limit the method of claim 9 to further include a method step, or intends to limit a previously recited “further including” step, therefore claim 18 is indefinite.

Claim 19 recites the phrase “wherein plurality” in line 1, which is nonsensical. The claim appears to be missing one or more words in line 1. As it is unclear what limitation is intended, claim 19 is indefinite.

Claim 21 recite the phrase “said clustered stacks” in line 1, which lacks antecedent basis. None of parent claims 1, 9, 18, 19 or 21 recites “clustered stacks” nor a step of “clustering stacks”, thus claim 21 is indefinite.

Claim 22 recites the term “said process” in line 3, which lacks antecedent basis. It is unclear what is intended as “the process”; i.e. the entire method, one or more individual steps, or some other “process”, therefore the claims are indefinite.

Claim 22 recites the term “said list” in lines 3-4, which lacks antecedent basis. No parent claim recites a “list” anywhere, thus claim 22 is indefinite.

Claim 22 limits the method of 21 to one wherein stacks “are eliminated” and a process “is repeated”. It is unclear if applicant intends steps of elimination and repetition to be active method steps, or intends some limitations of the stacks, therefore claim 22 is indefinite.

Claim 23 recite an apparent limitation of claim 1, but fails to recite any active method step or a clear (further) limitation of any step of claim 1. If applicant intends "generation" of a random set of amino acid sequences, then it is further unclear where in the method of claim 1 this step is intended to occur. It is noted that claim 1 does not recite amino acid "sequences" anywhere. As the limitation(s) intended for claim 23 are unclear, the claim is indefinite.

Claim 23 recites that sequences are generated "based on" binary sequences. It is unclear what parameters are to be considered, and to what degree, in order to "base" sequence generation "on" binary sequences, therefore the claim is indefinite.

Claim 24 limits claim 23 to one wherein an amino acid sequence "is reduced" to hydrophobicities. It is unclear whether "reduction" is intended to be an active method step, and if so, where in the method of claim 23 this step is intended to occur, and/or whether the reduction step is intended to further limit a method step of a parent claim. Further, it is unclear what is intended by a "reduction" of an amino acid sequence. Does applicant intend an in silico representation of a chemical reaction (e.g. redox-type of reduction using hydrophobic residues), or a decrease in size (such that the sequence become hydrophobic), or a subtraction of particular elements (side chains, atoms, etc., which are not hydrophobic). It is noted that any of these may be represented in some manner by "hydrophobicities" of individual amino acids, therefore the recitation that a sequence be "reduced to...hydrophobicities" does not clarify the intended limitation.

Claim 28 recites the phrase "with said stack as the lowest energy state", which is nonsensical. The claim further recites that some limitation "is larger than the average

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number of sequences per stack" in lines 2-3. It is unclear what is intended to be "larger than the average..." Claim 28 recites that a stack "is identified" in lines 1-2. It is unclear whether this is intended to be an active method step or some limitation of a stack. As none of the limitations of claim 28 are clear, claim 28 is indefinite. The limitations of claim 28 are so unclear that the examiner can not make any interpretation of the claim, therefore claim 28 is deemed unsearchable and will not be further examined on its merits with regard to the prior art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 15, 20 and 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by DAHIYAT et al. (Science (1997), vol. 278, pp. 82-87)

DAHIYAT teaches a method of identifying protein backbone configurations which are different from those of a known protein (i.e. a "novel" configuration) wherein a fixed number of secondary structural elements are specified (beta sheet, helix, and turn), a set of stacks (or configurations) comprising these elements is generated and evaluated (pp. 84-85), those stacks (configurations) which do not match a "known" structure are identified and displayed. See p. 86, middle column, last paragraph, which teaches that

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the $\beta\beta\alpha$ fold is different from those used to develop the methodology (i.e. different from a "known" configuration) and teaches that this represents a "new" (novel) motif. Fig. 6 is a display of the newly designed backbone configuration. Thus, claims 1-5 are anticipated. DAHIYAT teaches that his structure comprises at least one helix, two beta sheets and at least one turn; a total of four sets of secondary structural elements (Fig. 2), thereby anticipating claim 6. DAHIYAT's helix comprises at least twelve amino acids (Fig. 4), therefore claim 7 is anticipated. DAHIYAT assesses configurations relative to solvent accessible surface residues, specifically with regard to water (pp. 82 and 87), thus claims 15 and 25 are anticipated. Each structural element is grouped into a cluster or clusters (Fig. 4), therefore claim 20 is anticipated. DAHIYAT applies a variety of constraints in his design, including protein-folding and rms measurements (p. 85, third column), and specifically includes both hydrophobic and hydrophilic amino acid variables in his algorithm (p. 82), thereby anticipating claim 23.. He teaches that certain positions are restricted to hydrophobic residues, which represents "reduction to hydrophobicities" and anticipates claim 24.

Applicant's arguments filed 11/23/05 have been fully considered but they are not persuasive. In response to the argument that DAHIYAT does not teach generation of novel backbone configurations, but starts with a known invariant backbone configuration, it is noted the claims do not recite any step of generating novel backbone configurations. Amended claim 1 recites generating a set of stacks comprising specified amino acid secondary structural elements. Neither the set of stacks nor the secondary structural elements are limited to be new or "novel". Step (d) of claim 1

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recites *identifying* a set of stacks (note, NOT a backbone configuration) which has “no known counterpart”. As set forth above, it is unclear what a “known counterpart” is. However, DAHIYAT does teach identifying a combination of secondary structural elements (i.e. a set of stacks) which is different from other, known, structures and is a new “novel” motif, as set forth above. Thus, contrary to applicant’s arguments, DAHIYAT does teach at least identification of a novel backbone configuration. As DAHIYAT teaches all the limitations of the claims, as set forth above, the examiner maintains that DAHIYAT anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 9-11, 15-16, 20, 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over DAHIYAT et al. (Science (1997), vol. 278, pp. 82-87), as applied to claims 1-7, 15, 20 and 23-25 above, in view of DAHIYAT et al. (US 6,403,312).

Applicant’s arguments filed 11/23/05 have been fully considered but they are not persuasive. Applicant argues that DAHIYAT (1997) does not teach all the claimed limitations, and that DAHIYAT (‘312) does not remedy the deficiencies of DAHIYAT

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(1997). Again, it is noted that applicant's argument are directed to limitations not recited in the claims. The instant claims do not recite identification or "previously unknown, realizable backbone configurations" nor "means for designing protein backbone configurations" as set forth on page 15 of the response. The examiner maintains that DAHIYAT (1997) teaches the method of claims 1-7, 15, 20, 23-25, as set forth above, and therefore maintains that DAHIYAT (1997) and DAHIYAT ('312) make obvious the claims for the reasons and motivations previously set forth.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
2/21/04